19.03.28 - APCRA TC

1. **Welcome and roll call (Maureen) (5 min)**
2. **Case studies**
   a. **Overview (Tara) (5 min)**

Overview in order to address questions related to submissions - rolling basis, reviewed mainly to give constructive feedback and make sure it fits into the APCRA criteria (need for interagency collaboration, fit into the APCRA goals (below))

- Aim is to promote collaboration and dialogue on the scientific and regulatory needs for the application and acceptance of NAMs in regulatory decision making.
- Criteria for collaborative case studies include the use of a NAM in a clear regulatory application and the involvement of multiple regulatory agencies
   a. **Existing (those ongoing prior to October 2018 meeting)** *(oral presentation only; can share more detailed materials if available)*(Case study leads, 5 min each)
      i. **Retrospective** – Katie Paul-Friedman

Presented at SOT to show the connection btw retro and prospective (added to share drive); won best abstract from RASS; wrapping it up, paper in internal review at all Agencies. Reviews concluded by May it's the target. **All: please send journal suggestions to Katie Paul-Friedman.**

      ii. **Prospective** – Tomasz Sobanski

Last meeting in December - decided on Phase 2 testing. In vivo testing on 2 substances - teleconference in 2 weeks time. Not much update at this time. Impact of govt shutdown on EPA data generation.

      iii. **NAM Chemical Categorization (DDG)** – Dan Chang

Impact of govt shutdown. Upcoming team meeting for documentation of status, next steps. Two new members - Kellie Fay and Martin Phillips.

      iv. **Exposure** – Kristin Isaacs (unavailable for today's call; see written update below); HC is looking for the additional funds; limited calls due to EPA shutdown

Evaluation of ORD Functional Use Models

-Before Christmas ECHA provided a list of over 400 non-confidential polymer additives (stabilizers, UV absorbers, colorants, flame retardants) to EPA with their technical functions. We have run our "quantitative structural use relationship" (QSUR) classification models for ~250 chemicals for which we could obtain structures and descriptors. These predictions were provided back to ECHA this week. The models performed well, but we had an issue that many of the non-confidential chemicals were in the training set for the models. We will have a call with ECHA to discuss next steps: possibilities include obtaining additional classes or lists chemicals from ECHA such as a list of "suspected" polymer additives, or curation of additional structures from this list so we can run the models on the ~150 chemicals for which we could not obtain descriptors.

Evaluation of ORD Exposure Models with CMP Exposure Assessments

We are continuing to evaluate the CMP predictions against EPA models by chemical-product pair. Currently looking at route-specific exposures (dermal, inhalation, ingestion) among CMP, SHEDS-High Throughput, and EPA's Human Exposure Model (HEM). HEM is currently undergoing a case-study evaluation based on the CMP products and chemicals, contract mechanism is in place for those runs to be performed. Health Canada may have additional resources this year to support comparisons as well.

Exposure NAM Landscape Paper
Paper is in draft status; circulation to co-authors in the next quarter.

     v.   **Other?** –Philippe Hubert/Kristan Markey on the Endocrine/Thyroid case study
     Thyroid: had a meeting at end of October; govt shutdown impacts; go ahead to begin
     to concretely work on gathering information for the thyroid - analyze the literature
     data; pilot study within EPA using evidence mapping pilot to begin identifying relevant
     areas in thyroid pathway.
     EDNAM: catalogue of EDNAM tools - meeting in Europe and connected this study with
     a student that will complete the catalogue; CAAT, Univ in Italy, beginning of next year.

b. **Proposed/new starts (those proposed at or after the October 2018 meeting)** *(oral presentation only; can share more detailed materials if available)* (Case study leads, 5 min each)

     i.   **Zebrafish** – Cindy Woodland
     Finished first stage since October; building on the model and refining it for RA;
     evaluating for general toxicity/behavior for EDC (adipogenesis). NTP collaboration;
     20 compounds from NTP list; effects of existence of chorionic membrane impact on
     bioavailability; slide deck for most relevant information for technical aspects (list of
     compounds, protocols, etc). Final report just sent today - results for phenotyping,
     etc. Next phase starts on Monday - additional 10 substances. Working with ECCC;
     2019/20 -looking at kinetics. Compare with rodent data down the road. (slides
     added to share drive)

     ii.   **Eco-BER** – John Prindiville (Cristina Inglis will be away)
     ECHA, EPA (MED), ECCC (Jason O'Brien), JRC, US ACE (IVIVE), Germany, USGS
     Broader kickoff call (shutdown impact) - positive interest so far. Additional interest
     expressed from Jean-Lou Dorne, and US EPA - Kellie Fay (OCSPP)

     iii. **Eco-NAM** – Mark Viant
    Multi-omics and machine learning with Daphnia as model system. 10 chemical
analysis; partner reach out (ECCC, EPA (Adam Biales), Japan) and interest from other
partners. Exploring the opportunities.
Substance groups being proposed based on guideline of ECHA, others.
Prioritized - azo dyes; useful work with HC/Tara on this topic.
DMSO-based. Just finishing sourcing, final selection etc. ECHA/Univ Birmingham
phase to be completed by end of 2019.
Dan Villeneuve – interest with collaboration out of US EPA/MED. Kellie Fay (US
EPA/OPPT) may also contribute, particularly on chemical selection. Follow-on call to
be arranged.

     iv. **PFAS** – Julie Bourdon-Lacombe
    Link in vitro human cells for read across, etc. ASTAR, HC, in vitro in human cells with
TK data, PODs, RA, additivity strategies; HC - gene expression profiles for 30 PFAS (liver);
James from ASTAR - tk using IVIVE - working to understand half-lives impact. Predict
intracellular levels, link PK, PD data. ASTAR also looking at lung toxicity data.
Chemical selection? Crosswalk with EPA effort? Provide the list from Comptox
Dashboard.

b. **New proposals, or discussion of topic areas that would benefit from a case study**
(Tara) (15 min)
     • Here is the list from the Ottawa meeting:
         1. Genotoxicity
         2. Cross-species extrapolation

3. Mixtures
4. Crosswalk btw in vitro thyroid and apical endpoints

Possible new proposals – ECCC, possibly led by Jason O'Brien (not available for today's call)

Philippe - nice to have some people working on mathematical tools/in silico efforts.

Dan V - ecoBER - can look at mixtures there as well.

Jean-Lou - mixtures publication this week.

[HYPERLINK "https://www.efsa.europa.eu/en/press/news/190325"]

HC - combination of assays for genotoxicity being discussed internally.

Dale - definitely in this theme in relating NAMs to more traditional approaches - species extrapolation for eco, and invertebrates.

Lidka - Eurons project - additional resources, collaborators. More details needed.

1. **Communication Suggestions** (Mike) (15 min)

Communication suggestions follow-up from the Ottawa meeting.

 a. Public facing website – not yet live, but in process (ECHA)
  Far from having the physical website. If people have alternative ideas, happy to hear.

 b. Annual webinar-type interaction (separate from the F2F)

 c. Continued presentations at other meetings
  Please share any details/pdfs of presentations related to APCRA.

 d. Continued publications
  Please share any details/pdfs of publications related to APCRA.

 e. Other ideas or suggestions?
  All: Please send feedback to Maureen Gwinn (gwinn.maureen@epa.gov).

1. **APCRA-4** (Rusty) (5 min)

 a. Dates: October 9-11, 2019 (calendar invitation to follow)

 b. Location: Research Triangle Park, North Carolina, USA

 c. Proposed design: One day for case study teams to meet separate from the Face-to-Face (9 Oct), followed by Face-to-Face meeting (10-11 Oct).

- Feedback on the public stakeholder session from 2018: US - good feedback. No European feedback.
- Agenda to be discussed on next teleconference. Please send agenda topic ideas to Maureen.
- Organize the topics and a framework for how these proposals interact with each other. Add in some cohesiveness and lay them out in a way.
- Discussions with some industry - ecoMIE, chemical partitioning with ionizable, etc
- Mechanisms to present the industry work to APCRA?
  - Discuss at the next call/meeting.
  - with a dedicated webinar can improve how this is presented.
- Communications - link something to a meeting like SOT, satellite session elsewhere, or have a FutureTox meeting. Possibly SETAC, WorldCongress.
  - **All:** Please send further suggestions to Maureen Gwinn.

1. **Additional topics** (All, time permitting)
2. **Next meeting** (Maureen)

 Look for a doodle poll for a late May meeting.